Sheet <u>1</u> of <u>4</u>

Substitute Form PTO-1399 S. Department of Commerce (Modified)

Information Disclosure Statement by Applicant (Use several sheets if necessary)

(37 CFR §1.98(b))

Attorney's Docket No. (09531-016002 10/031,005

Application No. 10/031,005

Applicant Gary L. Nelsestuen

Filing Date October 29, 2001 1646

U.S. Patent Documents							
Examiner Initial	Desig. ID	Patent Number	Issue Date	Patentee	Class	Subclass	Filing Date If Appropriate
#5	AA	5,093,317	03/03/92	Lewis et al.	514	12	
13	AB	5,258,288	11/02/93	Wydro et al.	435	69.6	-
B	AC	5,288,629	02/22/94	Berkner	435	REGE	VED
15	AD	5,504,064	04/02/96	Morrissey et al.	514	BIN 1 2	2002
H5	AE	5,516,640	05/14/96	Watanabe et al.	435	7.4	2002
HS.	AF	5,580,560	12/03/96	Nicolaisen et al.	424	H CENTER	600;2900
HS	AG	5,788,965	08/04/98	Berkner et al.	424	.94.64	
135	АН	5,817,788	10/06/98	Berkner et al.	534	23.2	
彬	Al	5,824,639	10/20/98	Berkner	514	12	
113	AJ	5,833,982	11/20/98	Berkner et al.	424	94.64	
15	AK	5,837,843	11/17/98	Smirnov et al.	536	23.5	
内	AL	5,847,085	12/08/98	Esmon et al.	530	381	
B	AM	5,861,374	01/19/99	Berkner et al.	514	8	
15	AN	6,017,882	01/25/00	Nelsestuen	514	12	

Foreign Patent Documents or Published Foreign Patent Applications								
Examiner	Desig.	Document	Publication	Country or			Trans	slation
Initial	ID	Number	Date	Patent Office	Class	Subclass	Yes	No
#5	AO	0 296 413 A2	12/28/88	ЕРО	_			
\$13	AP	0 354 504 A2	02/14/90	EPO				
#3	AQ	WO 99/20767	04/29/99	PCT	T			

Other Documents (include Author, Title, Date, and Place of Publication)					
Examiner	Desig.				
Initial	ID	Document			
45	AR	Arnlijots et al., "Prevention of experimental arterial thrombosis by topical administration of active site-inactivated factor VIIa," J. Vasc. Surg., 1997, 25(2):341-346			
K	AS	Bauer, "Treatment of factor VII deficiency with recombinant factor VIIa," <u>Haemostasis</u> , 1996, 26(Suppl. 1):155-158			
43	ΑŤ	Broze et al., "Monoclonal anti-human factor VII antibodies. Detection in plasma of a second protein antigenically and genetically related to factor VII," J. Clin. Invest., 1985, 76:937-946			
HS	AU	Choudhri et al., "Targeted Inhibition of Intrinsic Coagulation Limits Cerebral Injury in Stroke without Increasing Intracerebral Hemorrhage," J. Exp. Med., 1999, 190:91-99			
Evaminar Sina	-4				

Examiner Signature

Date Considered

9-28-05

EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute Form P10-14-8N

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Information Disclosure Statement

by Applicant

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(37 CFR §1.98(b))

Sheet 2 of 4

Attorney's Docket No. 09531-016002

Applicant

Gary L. Nelsestuen

Filing Date
October 29, 2001

October 29, 2001

Other Documents (include Author, Title, Date, and Place of Publication)					
Examiner	Desig.				
Initial	ID	Document Cabo			
۱ ۸ -	AV	Christiansen et al., "Hydrophobic Amino Acid Residues of Human Anticoagulation Protein C that Contribute to its Functional Binding to Phospholipid Vesicles," <u>Biochemistry</u> , 1995, 34:10376-			
NO	AV	10382			
X13	AW	Dackiw et al., "Prevention of endotoxin-induced mortality by antitissue factor immunization," <u>Arch. Surg.</u> , 1996, 131:1273-1278			
AS	AX	Dahlback, "Inherited Thrombophilia: Resistance to Activated Protein C as a Pathogenic Factor of Venous Thromboemolism," Blood, 1995, 85:607-614			
43	AY	Esmon et al., "Isolation of a membrane-bound cofactor for thrombin-catalyzed activation of protein C," J. Biol. Chem., 1982, 257:859-864			
B	AZ	Evans, Jr. and Nelsestuen, "Importance of cis-Proline 22 in the Membrane-Binding Conformation of Bovine Prothrombin," <u>Biochemistry</u> , 1996, 35:8210-8215			
#5	AAA	Evans and Nelsestuan, "Importance of Cis-Proline 22 and the Aromatic Stack (Residues 41-45) for Prothrombin-Membrane Binding," Protein Sci., 1996, 5(Suppl. 1):163, Abstract #606-S			
45	ABB	Felgner et al., "Lipofection: a highly efficient, lipid-mediated DNA-transfection procedure," Proc. Natl. Acad. Sci. USA, 1987, 84:7413-7417			
45	ACC	Fiore et al., "The biochemical basis for the apparent defect of soluble mutant tissue factor in enhancing the proteolytic activities of factor VIIa," J. Biol. Chem., 1994, 269:143-149			
AS	ADD	Freedman et al., "Identification of the phospholipid binding site in the vitamin K-dependent blood coagulation protein factor IX," J. Biol. Chem., 1996, 271(27):16227-16236			
45	AEE	Furie and Furie, "The molecular basis of blood coagulation," Cell, 1988, 53:505-518			
45	AFF	Han et al., "Isolation of a protein Z-dependent plasma protease inhibitor," Proc. Natl. Acad. Sci. USA, 1998, 95:9250-9255			
No.	AGG	He et al., "Expression and functional characterization of chimeras between human and bovine vitamin-K-dependent protein-S-defining modules important for the species specificity of the			
B	7.00	activated protein C cofactor activity," Eur. J. Biochem., 1995, 227:433-440			
岁	АНН	Hedner et al., "Recombinant Activated Factor VII in the Treatment of Bleeding Episodes in Patients with Inherited and Acquired Bleeding Disorders," <u>Transfus. Med. Rev.</u> , 1993, 7:78-83			
.1.		Hope et al., "Production of Large Unilamellar Vesicles by a Rapid Extrusion Procedure.			
	All	Characterization of Size Distribution, Trapped Volume and Ability to Maintain a Membrane Protential," Biochem. Biophys. Acta, 1985, 812:55-65			
45	AJJ	Hoskins et al., "Cloning and characterization of human liver cDNA encoding a protein S precursor," Proc. Natl. Acad. Sci. USA, 1987, 84:349-353			
1	AKK	Huang, Biochemistry, 1969, 8:344-352			
KS	ALL	Humphries et al., "Chemical methods of protein synthesis and modification," <u>Curr. Opin.</u> <u>Biotechnol.</u> , 1991, 2(4):539-543			
*	AMM	Lu and Nelsestuen, "Dynamic Features of Prothrombin Interation with Phospholipid Vesicles of Different Size and Composition: Implications for Protein – Membrane Contact," <u>Biochemistry</u> , 1996, 35:8193-8200			
#5	ANN	Lu and Nelsestuen, "The prothrombinase reaction: "mechanism switching" between Michaelis- Menten and non-Michaelis-Menten behaviors," <u>Biochemistry</u> , 1996, 35:8201-8209			
K	AOO	Matsubara et al., "A receptor tyrosine kinase, Sky, and its ligand Gas 6 are expressed in gonads and support primordial germ cell growth or survival in culture," <u>Dev. Biol.</u> , 1996, 180:499-510			
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Examiner Signature	Date Considered 9-28-05
EXAMINER: Initials citation considered. Draw line through citation if no	t in conformance and not considered. Include copy of this form with

Substitute Disclosure Form (PTO-1449)

Sheet <u>3</u> of <u>4</u>

Substitute Form PTO-1449 (Modified)

(37 CFR §1.98(b))

U.S. Department of Commerce Patent and Trademark Office

Attorney's Docket No. 09531-016002

Application CEIVE

Information Disclosure Statement
by Applicant
(Use several sheets if necessary)

Applicant
Gary L. Nelsestuen

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Filing Date October 29, 2001 Group EUNICENTER 1600/290

Initial ID		Other D	ocuments (include Author, Title, Date, and Place of Publication)
App Mayer et al., "Prothrombin Association with Phospholipid Monolayers," <u>Biochemistry</u> , 1983, 22(2):316-321  AQQ Michonald et al., "Comparison of Naturally Occurring Vitamin K-dependent Proteins: Correlation of Amino Acid Sequences and Membrane Binding Properties Suggests a Membrane Contact Site," <u>Michonald et al.</u> , "Ionic Properties of Membrane Association by Vitamin K-Dependent Proteins: The Case for Univalency," <u>Biochemistry</u> , 1997, 36(50):15589-15598  ASS McDonald et al., "Ionic Properties of Membrane Association by Vitamin K-Dependent Proteins: The Case for Univalency," <u>Biochemistry</u> , 1997, 36(50):1589-15598  ASS Michonald et al., "Ionic Properties of Membrane Association by Vitamin K-Dependent Proteins: The Case for Univalency," <u>Biochemistry</u> , 1997, 36(50):1589-15598  ASS Michonald et al., "Ionic Properties of Acid Acid Care VII Levils in Plasma Using a Tissue Factor Mutant Selectively Deficient in Promoting Factor VII Activation," <u>Blood</u> , 1993, 81(3):734-744  ATT Muir et al., "The chemical synthesis of proteins," <u>Curr. Opin. Biotechnol.</u> , 1993, 4(4):420-427  Nakagaki et al., "Initiation of the Extrinsic Pathway of Blood Coagulation: Evidence for the Tissue Factor Dependent Autoactivation of Human Coagulation Factor VII," <u>Biochem. Biophys. Res. Commun.</u> , 1971, 45:198-203  AVV Destestuen and Suttie, "Properties of Asialo and Aglycoprothrombin," <u>Biochem. Biophys. Res. Commun.</u> , 1971, 45:198-203  AWW Bioling," <u>Biochemistry</u> , 1977, 16(19):4164-4171  Micolases et al., "A prothrombinase-based assay for detection of resistance to activated protein C," <u>Thromb. Haemost.</u> , 1996, 76:200-204  AZZ Micolases et al., "A prothrombinase-based assay for detection of resistance to activated protein C," <u>Thromb. Haemost.</u> , 1996, 76:200-204  AZZ Micolases et al., "Immunological aspects of recombinant factor VIIa (rFVIIa) in clinical use," <u>Thromb. Haemost.</u> , 1996, 76:200-204  AZZ Micolases et al., "Grans-cis Isomerization of Froline 22 in Bovine Prothrombin Fragment 1: A Surprising Result of Structural Characteriz	Examiner		Document
Amino Acid Sequences and Membrane Binding Properties Suggests a Membrane Contact Site," Biochemistry, 1997, 36:5120-5127  ARR McDonald et al., "Ionic Properties of Membrane Association by Vitamin K-Dependent Proteins: The Case for Univalency," Biochemistry, 1997, 36:50):15589-15598  ASS Morrissey et al., "Quantitation of Activated Factor VII Levels in Plasma Using a Tissue Factor Mutant Selectively Deficient in Promoting Factor VII Activation," Blood, 1993, 81(3):734-744  ATT Muir et al., "The chemical synthesis of proteins," Curr. Opin. Biotechnol., 1993, 4(4):420-427  Nakagaki et al., "Initiation of the Extrinsic Pathway of Blood Coagulation: Evidence for the Tissue Factor Dependent Autoactivation of Human Coagulation Factor VII," Biochemistry, 1991, 30:10819-10824  AVV Nelsestuen and Suttie, "Properties of Asialo and Aglycoprothrombin," Biochem. Biophys. Res. Commun., 1971, 45:198-203  AWW Nelsestuen et al., "Equilibria Involved in Prothrombin-and Blood Clotting Factor X-Membrane Binding," Biochemistry, 1977, 16(19):4164-4171  Nicolaes et al., "A prothrombinase-based assay for detection of resistance to activated protein C," Thromb. Haemost., 1996, 76:404-410  AXX Nicolaes et al., "Immunological aspects of recombinant factor VIIa (rFVIIa) in clinical use," Thromb. Haemost., 1996, 76:200-204  AZZ Perera et al., "Trans-cis Isomerization of Proline 22 in Bovine Prothrombin Fragment 1: A Surprising Result of Structural Characterization," Biochemistry, 1998, 37:10920-10927  AAAA Persson and Nielsen, "Site-directed mutagenesis but not gamma-carboxylation of Glu-35 in factor VIIa affects the association with tissue factor," FEBS Letters, 1996, 385(3):241-243  Petersen et al., "Quenching of the amidolytic activity of one-chain tissue-type plasminogen activator by mutation of lysine-416," Biochemistry, 1990, 29:3451-3457  ACCC Rateliffe et al., "The Importance of Specific y-Carboxyglutamic Acid Residues in Prothrombin," J. Biol. Chem., 1993, 268(32):2439-24345  AFFF Schulman et al., "Forein Structural Requirements an			Mayer et al., "Prothrombin Association with Phospholipid Monolayers," Biochemistry, 1983,
ASS Morrissey et al., "Quantitation of Activated Factor VII Levels in Plasma Using a Tissue Factor Mutant Selectively Deficient in Promoting Factor VII Activation," Blood, 1993, 81(3):734-744  ATT Muir et al., "The chemical synthesis of proteins," Curr. Opin. Biotechnol., 1993, 4(4):420-427  AUU Nakagaki et al., "Initiation of the Extrinsic Pathway of Blood Coagulation: Evidence for the Tissue Factor Dependent Autoactivation of Human Coagulation Factor VII," Biochemistry, 1991, 30:10819-10824  AVV Nelsestuen and Suttie, "Properties of Asialo and Aglycoprothrombin," Biochem. Biophys. Res. Commun., 1971, 45:198-203  AWW Binding," Biochemistry, 1977, 16(19):4164-4171  AXX Nicolaes et al., "Faquilibria Involved in Prothrombin- and Blood Clotting Factor X-Membrane Binding," Biochemistry, 1977, 16(19):4164-4171  AXY Nicolaes et al., "A prothrombinase-based assay for detection of resistance to activated protein C," Thromb. Haemost., 1996, 76:404-410  AYY Nicolaisen et al., "Immunological aspects of recombinant factor VIIa (rFVIIa) in clinical use," Thromb. Haemost., 1996, 76:200-204  Perera et al., "Trans-cis Isomerization of Proline 22 in Bovine Prothrombin Fragment 1: A Surprising Result of Structural Characterization," Biochemistry, 1998, 37:10920-10927  Person and Nielsen, "Site-directed mutagenesis but not gamma-carboxylation of Glu-35 in factor VIIa affects the association with tissue factor," FEBS Letters, 1996, 385(3):241-243  Petersen et al., "Quenching of the amidolytic activity of one-chain tissue-type plasminogen activator by mutation of lysine-416," Biochemistry, 1990, 29:3451-3457  ACCC Biol. Chem., 1993, 268(32):24339-24345  ACCC Biol. Chem., 1993, 268(32):24339-24345  AFFF Schulman et al., "Prothrombin-Membrane Interaction. Effects of Ionic Strength, pH, and Temperature," Biochemistry, 1980, 19(13):3028-3033  Rezaie and Esmon, "The function of calcium in protein C activation by thrombin and the thrombin-thrombomodulin complex can be distinguished by mutational analysis of protein C derivatives," J. Bio	X	AQQ	McDonald et al., "Comparison of Naturally Occurring Vitamin K-dependent Proteins: Correlation of Amino Acid Sequences and Membrane Binding Properties Suggests a Membrane Contact Site," <u>Biochemistry</u> , 1997, 36:5120-5127
Mutant Selectively Deficient in Promoting Factor VII Activation," Blood, 1993, 81(3):734-744  Muir et al., "The chemical synthesis of proteins," Curr. Opin. Biotechnol., 1993, 4(4):420-427  Nakagaki et al., "Initiation of the Extrinsic Pathway of Blood Coagulation: Evidence for the Tissue Factor Dependent Autoactivation of Human Coagulation Factor VII," Biochem. Biophys. Res. Commun., 1971, 45:198-203  Nelsestuen and Suttie, "Properties of Asialo and Aglycoprothrombin," Biochem. Biophys. Res. Commun., 1971, 45:198-203  Nelsestuen et al., "Equilibria Involved in Prothrombin- and Blood Clotting Factor X-Membrane Binding," Biochemistry, 1977, 16(19):4164-4171  AXX Nicolase et al., "A prothrombinase-based assay for detection of resistance to activated protein C," Thromb. Haemost., 1996, 76:404-410  Nicolaisen et al., "Immunological aspects of recombinant factor VIIa (rFVIIa) in clinical use," Thromb. Haemost., 1996, 76:200-204  Perera et al., "Trans-cis Isomerization of Proline 22 in Bovine Prothrombin Fragment 1: A Surprising Result of Structural Characterization," Biochemistry, 1998, 37:10920-10927  Person and Nielsen, "Site-directed mutagenesis but not gamma-carboxylation of Glu-35 in factor VIIa affects the association with tissue factor," FEBS Letters, 1996, 385(3):241-243  Person and Nielsen, "Site-directed mutagenesis but not gamma-carboxylation of Glu-35 in factor VIIa affects the association with tissue factor," FEBS Letters, 1996, 385(3):241-243  Person and Nielsen, "Site-directed mutagenesis but not gamma-carboxylation of Glu-35 in factor VIIa affects the association with tissue factor," FEBS Letters, 1996, 385(3):241-243  ABBB Resnick and Nelsester, "Site-directed mutagenesis but not gamma-carboxylation of Glu-35 in factor VIIa affects the association with tissue factor," FEBS Letters, 1996, 385(3):241-243  ACCC Research and Nelsen, "Site-directed mutagenesis but not gamma-carboxylation of Glu-35 in factor VIIa affects the association with tissue factor," FEBS Letters, 1996, 385(3):241-243  Resnick and	W3	ARR	Case for Univalency," <u>Biochemistry</u> , 1997, 36(50):15589-15598
AUU AUU AUU AUU AUU AUU AUU AVV	45	ASS	Morrissey et al., "Quantitation of Activated Factor VII Levels in Plasma Using a Tissue Factor Mutant Selectively Deficient in Promoting Factor VII Activation," <u>Blood</u> , 1993, 81(3):734-744
AUU Stactor Dependent Autoactivation of Human Coagulation Factor VII," Biochemistry, 1991, 30:10819-10824  AVV Nelsestuen and Suttie, "Properties of Asialo and Aglycoprothrombin," Biochem. Biophys. Res. Commun., 1971, 45:198-203  AWW Nelsestuen et al., "Equilibria Involved in Prothrombin- and Blood Clotting Factor X-Membrane Binding," Biochemistry, 1977, 16(19):4164-4171  AXX Nicolase et al., "A prothrombinase-based assay for detection of resistance to activated protein C," Thromb. Haemost., 1996, 76:404-410  AYY Nicolasien et al., "Immunological aspects of recombinant factor VIIa (rFVIIa) in clinical use," Thromb. Haemost., 1996, 76:200-204  AZZ Perera et al., "Trans-cis Isomerization of Proline 22 in Bovine Prothrombin Fragment 1: A Surprising Result of Structural Characterization," Biochemistry, 1998, 37:10920-10927  AAAA ABBB Petersen and Nielsen, "Site-directed mutagenesis but not gamma-carboyaltion of Glu-35 in factor VIIa affects the association with tissue factor," FEBS Letters, 1996, 385(3):241-243  ABBB Petersen et al., "Quenching of the amidolytic activity of one-chain tissue-type plasminogen activator by mutation of lysine-416," Biochemistry, 1990, 29:3451-3457  ACCC ACCC ACCC ACCC Accc ACCC Accc Bateliffe et al., "The Importance of Specific γ-Carboxyglutamic Acid Residues in Prothrombin," J. Biol. Chem., 1993, 268(32):24392-24345  ADDD Resnick and Nelsestuen, "Prothrombin-Membrane Interaction. Effects of Ionic Strength, pH, and Temperature," Biochemistry, 1980, 19(13):3028-3033  ACCC Biol. Chem., 1992, 267:26104-26109  AFFF ASC2 AGGG Schulman et al., "The function of calcium in protein C activation by thrombin and the thrombin-thrombomodulin complex can be distinguished by mutational analysis of protein C derivatives," J. Biol. Chem., 1990, 29(34):7845-7852  AGGG Schulman et al., "Protein Structural Requirements and Properties of Membrane Binding by γ-Carboxyglutamic Acid-containing Plasma Proteins and Peptides," J. Biol. Chem., 1989, 264:20288-20296	30	ATT	
AWW Nelsestuen et al., "Equilibria Involved in Prothrombin- and Blood Clotting Factor X-Membrane Binding," Biochemistry, 1977, 16(19):4164-4171  AXX Nicolaise et al., "A prothrombinase-based assay for detection of resistance to activated protein C," Thromb. Haemost., 1996, 76:404-410  AYY Nicolaisen et al., "Immunological aspects of recombinant factor VIIa (rFVIIa) in clinical use," Thromb. Haemost., 1996, 76:200-204  AZZ Perera et al., "Trans-cis Isomerization of Proline 22 in Bovine Prothrombin Fragment 1: A Surprising Result of Structural Characterization," Biochemistry, 1998, 37:10920-10927  AAAA Person and Nielsen, "Site-directed mutagenesis but not gamma-carboxylation of Glu-35 in factor VIIa affects the association with tissue factor," FEBS Letters, 1996, 385(3):241-243  ABBB Petersen et al., "Quenching of the amidolytic activity of one-chain tissue-type plasminogen activator by mutation of lysine-416," Biochemistry, 1990, 29:3451-3457  ACCC Ratcliffe et al., "The Importance of Specific γ-Carboxyglutamic Acid Residues in Prothrombin," J. Biol. Chem., 1993, 268(32):24339-24345  ABDD Resnick and Nelsestuen, "Prothrombin-Membrane Interaction. Effects of Ionic Strength, pH, and Temperature," Biochemistry, 1980, 19(13):3028-3033  Rezaie and Esmon, "The function of calcium in protein C activation by thrombin and the thrombin-thrombomodulin complex can be distinguished by mutational analysis of protein C derivatives," J. Biol. Chem., 1992, 267:26104-26109  Schmidel et al., "Oranization of the Human Protein S Genes," J. Biol. Chem., 1990, 29(34):7845-7852  Schulman et al., "Feasibility of using recombinant factor VIIa in continuous infusion," Thromb. Haemost., 1996, 75(3):432-436  Schwalbe et al., "Protein Structural Requirements and Properties of Membrane Binding by γ-Carboxyglutamic Acid-containing Plasma Proteins and Peptides," J. Biol. Chem., 1989, 264:20288-20296	B	AUU	Factor Dependent Autoactivation of Human Coagulation Factor VII," Biochemistry, 1991, 30:10819-10824
AXX  Nicolase et al., "A prothrombinase-based assay for detection of resistance to activated protein C,"  Thromb. Haemost., 1996, 76:404-410  AYY  Nicolaisen et al., "Immunological aspects of recombinant factor VIIa (rFVIIa) in clinical use,"  Thromb. Haemost., 1996, 76:200-204  AZZ  Perera et al., "Trans-cis Isomerization of Proline 22 in Bovine Prothrombin Fragment 1: A  Surprising Result of Structural Characterization," Biochemistry, 1998, 37:10920-10927  Person and Nielsen, "Site-directed mutagenesis but not gamma-carboxylation of Glu-35 in factor  VIIa affects the association with tissue factor," FEBS Letters, 1996, 385(3):241-243  Petersen et al., "Quenching of the amidolytic activity of one-chain tissue-type plasminogen activator by mutation of lysine-416," Biochemistry, 1990, 29:3451-3457  ACCC  Ratcliffe et al., "The Importance of Specific γ-Carboxyglutamic Acid Residues in Prothrombin," J.  Biol. Chem., 1993, 268(32):24339-24345  Resnick and Nelsestuen, "Prothrombin-Membrane Interaction. Effects of Ionic Strength, pH, and Temperature," Biochemistry, 1980, 19(13):3028-3033  Rezaie and Esmon, "The function of calcium in protein C activation by thrombin and the thrombin- thrombomodulin complex can be distinguished by mutational analysis of protein C derivatives," J.  Biol. Chem., 1992, 267:26104-26109  Schmidel et al., "Coranization of the Human Protein S Genes," J. Biol. Chem., 1990, 29(34):7845- 7852  AGGG  Schwalbe et al., "Feasibility of using recombinant factor VIIa in continuous infusion," Thromb.  Haemost., 1996, 75(3):432-436  Schwalbe et al., "Protein Structural Requirements and Properties of Membrane Binding by γ- Carboxyglutamic Acid-containing Plasma Proteins and Peptides," J. Biol. Chem., 1989, 264:20288- 20296	45	AVV	Commun., 1971, 45:198-203
Thromb. Haemost., 1996, 76:404-410  AYY  Nicolaisen et al., "Immunological aspects of recombinant factor VIIa (rFVIIa) in clinical use," Thromb. Haemost., 1996, 76:200-204  AZZ  Perera et al., "Trans-cis Isomerization of Proline 22 in Bovine Prothrombin Fragment 1: A Surprising Result of Structural Characterization," Biochemistry, 1998, 37:10920-10927  Persson and Nielsen, "Site-directed mutagenesis but not gamma-carboxylation of Glu-35 in factor VIIa affects the association with tissue factor," FEBS Letters, 1996, 385(3):241-243  Petersen et al., "Quenching of the amidolytic activity of one-chain tissue-type plasminogen activator by mutation of lysine-416," Biochemistry, 1990, 29:3451-3457  ACCC  ACCC  Resnick and Nelsestuen, "Prothrombin-Membrane Interaction. Effects of Ionic Strength, pH, and Temperature," Biochemistry, 1980, 19(13):3028-3033  Rezaie and Esmon, "The function of calcium in protein C activation by thrombin and the thrombin-thrombomodulin complex can be distinguished by mutational analysis of protein C derivatives," J. Biol. Chem., 1992, 267:26104-26109  AFFF  AGGG  ACGG  Schmidel et al., "Geasibility of using recombinant factor VIIa in continuous infusion," Thromb. Haemost., 1996, 75(3):432-436  Schwalbe et al., "Protein Structural Requirements and Properties of Membrane Binding by γ-Carboxyglutamic Acid-containing Plasma Proteins and Peptides," J. Biol. Chem., 1989, 264:20288-20296	*	AWW	Binding," Biochemistry, 1977, 16(19):4164-4171
Thromb. Haemost., 1996, 76:200-204  Perera et al., "Trans-cis Isomerization of Proline 22 in Bovine Prothrombin Fragment 1: A Surprising Result of Structural Characterization," Biochemistry, 1998, 37:10920-10927  Persson and Nielsen, "Site-directed mutagenesis but not gamma-carboxylation of Glu-35 in factor VIIa affects the association with tissue factor," FEBS Letters, 1996, 385(3):241-243  ABBB Petersen et al., "Quenching of the amidolytic activity of one-chain tissue-type plasminogen activator by mutation of lysine-416," Biochemistry, 1990, 29:3451-3457  ACCC Ratcliffe et al., "The Importance of Specific γ-Carboxyglutamic Acid Residues in Prothrombin," J. Biol. Chem., 1993, 268(32):24339-24345  ADDD Resnick and Nelsestuen, "Prothrombin-Membrane Interaction. Effects of Ionic Strength, pH, and Temperature," Biochemistry, 1980, 19(13):3028-3033  Rezaie and Esmon, "The function of calcium in protein C activation by thrombin and the thrombin-thrombomodulin complex can be distinguished by mutational analysis of protein C derivatives," J. Biol. Chem., 1992, 267:26104-26109  AFFF Schmidel et al., "Oranization of the Human Protein S Genes," J. Biol. Chem., 1990, 29(34):7845-7852  AGGG Schulman et al., "Feasibility of using recombinant factor VIIa in continuous infusion," Thromb. Haemost., 1996, 75(3):432-436  Schwalbe et al., "Protein Structural Requirements and Properties of Membrane Binding by γ-Carboxyglutamic Acid-containing Plasma Proteins and Peptides," J. Biol. Chem., 1989, 264:20288-20296	K	AXX	Thromb. Haemost., 1996, 76:404-410
Surprising Result of Structural Characterization," Biochemistry, 1998, 37:10920-10927  Hersson and Nielsen, "Site-directed mutagenesis but not gamma-carboxylation of Glu-35 in factor VIIa affects the association with tissue factor," FEBS Letters, 1996, 385(3):241-243  ABBB Petersen et al., "Quenching of the amidolytic activity of one-chain tissue-type plasminogen activator by mutation of lysine-416," Biochemistry, 1990, 29:3451-3457  ACCC Ratcliffe et al., "The Importance of Specific γ-Carboxyglutamic Acid Residues in Prothrombin," J. Biol. Chem., 1993, 268(32):24339-24345  Resnick and Nelsestuen, "Prothrombin-Membrane Interaction. Effects of Ionic Strength, pH, and Temperature," Biochemistry, 1980, 19(13):3028-3033  Rezaie and Esmon, "The function of calcium in protein C activation by thrombin and the thrombin-thrombomodulin complex can be distinguished by mutational analysis of protein C derivatives," J. Biol. Chem., 1992, 267:26104-26109  AFFF Schmidel et al., "Oranization of the Human Protein S Genes," J. Biol. Chem., 1990, 29(34):7845-7852  Schulman et al., "Feasibility of using recombinant factor VIIa in continuous infusion," Thromb. Haemost., 1996, 75(3):432-436  Schwalbe et al., "Protein Structural Requirements and Properties of Membrane Binding by γ-Carboxyglutamic Acid-containing Plasma Proteins and Peptides," J. Biol. Chem., 1989, 264:20288-20296	K	AYY	<u>Thromb. Haemost.</u> , 1996, 76:200-204
VIIa affects the association with tissue factor," FEBS Letters, 1996, 385(3):241-243  ABBB Petersen et al., "Quenching of the amidolytic activity of one-chain tissue-type plasminogen activator by mutation of lysine-416," Biochemistry, 1990, 29:3451-3457  ACCC Ratcliffe et al., "The Importance of Specific γ-Carboxyglutamic Acid Residues in Prothrombin," J. Biol. Chem., 1993, 268(32):24339-24345  ADDD Resnick and Nelsestuen, "Prothrombin-Membrane Interaction. Effects of Ionic Strength, pH, and Temperature," Biochemistry, 1980, 19(13):3028-3033  Rezaie and Esmon, "The function of calcium in protein C activation by thrombin and the thrombin-thrombomodulin complex can be distinguished by mutational analysis of protein C derivatives," J. Biol. Chem., 1992, 267:26104-26109  Schmidel et al., "Oranization of the Human Protein S Genes," J. Biol. Chem., 1990, 29(34):7845-7852  AGGG Schulman et al., "Feasibility of using recombinant factor VIIa in continuous infusion," Thromb. Haemost., 1996, 75(3):432-436  Schwalbe et al., "Protein Structural Requirements and Properties of Membrane Binding by γ-Carboxyglutamic Acid-containing Plasma Proteins and Peptides," J. Biol. Chem., 1989, 264:20288-20296	#5	. AZZ	Surprising Result of Structural Characterization," Biochemistry, 1998, 37:10920-10927
by mutation of lysine-416," Biochemistry, 1990, 29:3451-3457  ACCC Ratcliffe et al., "The Importance of Specific γ-Carboxyglutamic Acid Residues in Prothrombin," J. Biol. Chem., 1993, 268(32):24339-24345  ADDD Resnick and Nelsestuen, "Prothrombin-Membrane Interaction. Effects of Ionic Strength, pH, and Temperature," Biochemistry, 1980, 19(13):3028-3033  Rezaie and Esmon, "The function of calcium in protein C activation by thrombin and the thrombin-thrombomodulin complex can be distinguished by mutational analysis of protein C derivatives," J. Biol. Chem., 1992, 267:26104-26109  AFFF Schmidel et al., "Oranization of the Human Protein S Genes," J. Biol. Chem., 1990, 29(34):7845-7852  AGGG Schulman et al., "Feasibility of using recombinant factor VIIa in continuous infusion," Thromb. Haemost., 1996, 75(3):432-436  Schwalbe et al., "Protein Structural Requirements and Properties of Membrane Binding by γ-Carboxyglutamic Acid-containing Plasma Proteins and Peptides," J. Biol. Chem., 1989, 264:20288-20296	뭥	AAAA	VIIa affects the association with tissue factor," FEBS Letters, 1996, 385(3):241-243
Biol. Chem., 1993, 268(32):24339-24345  ADDD Resnick and Nelsestuen, "Prothrombin-Membrane Interaction. Effects of Ionic Strength, pH, and Temperature," Biochemistry, 1980, 19(13):3028-3033  Rezaie and Esmon, "The function of calcium in protein C activation by thrombin and the thrombin-thrombomodulin complex can be distinguished by mutational analysis of protein C derivatives," J. Biol. Chem., 1992, 267:26104-26109  AFFF Schmidel et al., "Oranization of the Human Protein S Genes," J. Biol. Chem., 1990, 29(34):7845-7852  AGGG Schulman et al., "Feasibility of using recombinant factor VIIa in continuous infusion," Thromb. Haemost., 1996, 75(3):432-436  Schwalbe et al., "Protein Structural Requirements and Properties of Membrane Binding by γ-Carboxyglutamic Acid-containing Plasma Proteins and Peptides," J. Biol. Chem., 1989, 264:20288-20296	#S	ABBB	by mutation of lysine-416," Biochemistry, 1990, 29:3451-3457
Temperature," Biochemistry, 1980, 19(13):3028-3033  Rezaie and Esmon, "The function of calcium in protein C activation by thrombin and the thrombin-thrombomodulin complex can be distinguished by mutational analysis of protein C derivatives," J. Biol. Chem., 1992, 267:26104-26109  AFFF Schmidel et al., "Oranization of the Human Protein S Genes," J. Biol. Chem., 1990, 29(34):7845-7852  AGGG Schulman et al., "Feasibility of using recombinant factor VIIa in continuous infusion," Thromb. Haemost., 1996, 75(3):432-436  Schwalbe et al., "Protein Structural Requirements and Properties of Membrane Binding by γ-Carboxyglutamic Acid-containing Plasma Proteins and Peptides," J. Biol. Chem., 1989, 264:20288-20296	15	ACCC	Biol. Chem., 1993, 268(32):24339-24345
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AGGG Schulman et al., "Feasibility of using recombinant factor VIIa in continuous infusion," Thromb.  Haemost., 1996, 75(3):432-436  Schwalbe et al., "Protein Structural Requirements and Properties of Membrane Binding by γ- Carboxyglutamic Acid-containing Plasma Proteins and Peptides," J. Biol. Chem., 1989, 264:20288- 20296	its	AFFF	7852
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Seshadri et al., "Differences in the Metal Ion Structure between Sr- and Ca-Prothrombin Fragment	B	АННН	Carboxyglutamic Acid-containing Plasma Proteins and Peptides," J. Biol. Chem., 1989, 264:20288- 20296
1," <u>Biochemistry</u> , 1994, 33:1087-1092	#5	Alli	Seshadri et al., "Differences in the Metal Ion Structure between Sr- and Ca-Prothrombin Fragment 1," Biochemistry, 1994, 33:1087-1092

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Sheet <u>4</u> of <u>4</u>

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Application Por 10/031,005

Information Disclosure Statement by Applicant (Use several sheets if necessary)

Applicant Gary L. Nelsestuen

Filing Date October 29, 2001

		ocuments (include Author, Title, Date, and Place of Publication)
Examiner	Desig.	
Initial	ID	Document -
jks	AJJJ	Shah et al., "Manipulation of the membrane binding site of vitamin K-dependent proteins: Enhanced biological function of human factor VII," Proc. Natl. Acad. Sci. USA, 1998, 95(8):4229-4234
15	AKKK	Shen et al., "Enhancing the Activity of Protein C by Mutagenetis to Improve the Membrane-Binding Site: Studies Related to Proline 10," <u>Biochemistry</u> , 1997, 36(51):16025-16031
3	ALLL	Shen et al., "Enhancement of Human Protein C Function by Site-directed Mutagenesis of the γ-Carboxyglutamic Acid Domain," J. Biol. Chem., 1998, 273(47):31086-31091
#	АМММ	Smirnov et al., "A Chimeric Protein C Containing the Prothrombin Gla Domain Exhibits Increased Anticoagulant Activity and Altered Phospholipid Specificity," J. Biol. Chem., 1998, 273(15):9031-9040
33	ANNN	Sorensen et al., "Incorporation of an active site inhibitor in factor VIIa alters the affinity for tissue factor," J. Biol. Chem., 1997, 272(18):11863-11868
3	A000	Thariath et al., "Highly conserved residue arginine-15 is required for the Ca <sup>2+</sup> -dependent properties of the γ-carboxyglutamic acid domain of human anticoagulation Protein C and activated Protein C," <u>Biochem. J.</u> , 1997, 322:309-315
A	APPP	Thomsen et al., "Pharmacokinetics of recombinant factor VIIa in the rat – a comparison of bio-, immuno- and isotope assays," Thromb. Haemost., 1993, 70(3):458-464
AS	AQQQ	Vallette et al., "Construction of mutant and chimeric genes using the polymerase chain reaction," <u>Nucleic Acids Res.</u> , 1989, 17(2):723-733
B	ARRR	Vrana et al., "Expression of tissue factor in tumor stroma correlates with progression to invasive human breast cancer: paracrine regulation by carcinoma cell-derived members of the transforming growth factor beta family," Cancer Res., 56:5063-5070
*	ASSS	Weber et al., "Modifications of Bovine Prothrombin Fragment 1 in the Presence and Absence of Ca(II) Ions," J. Biol. Chem., 1992, 267(7):4564-4569
K	ATTT	Wei et al., "Kinetic and Mechanistic Analysis of Prothrombin-Membrane Binding by Stopped-Flow Light Scattering," Biochemistry, 1982, 21:1949-1959
8	AUUU	Welsch et al., "Chemical Modification of Prothrombin Fragment 1: Documentation of Sequential, Two-Stage Loss of Protein Function," <u>Biochemistry</u> , 1988, 27:4933-4938
ils	Αννν	Welsch and Nelsestuen, "Amino-terminal alanine functions in a calcium-specific process essential for membrane binding by prothrombin fragment 1," <u>Biochemistry</u> , 1988, 27:4939-4945
85	AWWW	Yan et al., "Characterization and Novel Purification of Recombinant Human Protein C from Three Mammalian Cell Lines," <u>Bio/Technology</u> , 1990, 8:655-661
X	AXXX	Zhang et al., "Role of Individual γ-Caboxyglutamic Acid Residues of Activated Human Protein C in Defining its In Vitro Anticoagulant Activity," <u>Blood</u> , 1992, 80(4):942-952
H	AYYY	Zhang et al., "The Contributions of Individual γ-Carboxyglutamic Acid Residues in the Calcium- dependent Binding of Recombinant Human Protein C to Acidic Phospholipid Vesicles," <u>J. Biol.</u> <u>Chem.</u> , 1993, 268(16):12040-12045
B	AZZZ	Zwaal et al., "Lipid-protein interactions in blood coagulation," <u>Biochimica et Biophysica Acta</u> , 1998, 1376:433-453

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Applicant
Gary L. Nelsestuen

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October 29, 2001

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U.S. Patent Documents							
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